

CLAIMS

What is claimed is:

1. A method for determining the susceptibility of an individual to a chronic obstructive pulmonary disorder (COPD), comprising the step of determining the presence of an exon 6 codon 279 Gln/Arg single nucleotide polymorphism within the matrix metalloproteinase-9 (MMP-9) locus in a biological sample obtained from the individual, wherein the 279 arginine polymorphism indicates susceptibility to chronic obstructive pulmonary disorder.

2. The method of claim 1, further comprising use of an isolated nucleic acid molecule to detect the codon 279 Gln/Arg single nucleotide polymorphism.

3. The method of claim 2, wherein the isolated nucleic acid molecule is DNA, cDNA or mRNA.

4. The method of claim 2, wherein the isolated nucleic acid molecule is a single-stranded or double-stranded nucleic acid molecule.

5. The method of claim 2, wherein the isolated nucleic acid molecule is a probe which hybridizes under stringent conditions to a particular allele of the polymorphism.

6. The method of claim 5, wherein the probe comprises the sequence 5'-CTCTACACCCGGGACGGCAATG (SEQ ID NO:1).

7. The method of claim 5, wherein the probe comprises the sequence 5'-ACTCTACACCCAGGACGGCAATGC (SEQ ID NO:2).

8. The method of claim 2, further comprising use of a nucleotide primer which amplifies a particular allele of the polymorphism.

9. The method of claim 8, wherein the nucleotide primer comprises a 5'-TCTCCCCCTTTCCACATC (SEQ ID NO:3) sense primer or a 5'-TGTGCTGTCTCCGCCTTCT (SEQ ID NO:4) antisense primer.

10. The method of claim 1, wherein determining the presence of an exon 6 codon 279 Gln/Arg single nucleotide polymorphism within the MMP-9 locus comprises testing expressed protein for the presence or absence of arginine in the 279 position.

11. A method of determining the efficacy of a substance to inhibit the 279Arg MMP-9 enzyme for use as a therapeutic or preventive agent for COPD, the method comprising the steps of:  
providing the 279Arg MMP-9 enzyme; and  
testing the substance for inhibition of the 279Arg MMP-9 enzyme.

5 12. The method of claim 11, wherein providing the 279Arg MMP-9 enzyme comprises inserting a gene expressing the 279Arg MMP-9 enzyme into a cell line.

13. The method of claim 12, wherein the gene expressing the 279Arg MMP-9 enzyme is SEQ ID NO:11 where 841 n is guanine (G).

10 14. The method of claim 11, further comprising the steps of:  
providing the 279Gln MMP-9 enzyme;  
testing the substance for inhibition of the 279Gln MMP-9 enzyme; and  
comparing the results obtained for inhibition of the 279Arg MMP-9 enzyme with results obtained for inhibition of the 279Gln MMP-9 enzyme.

15 15. The method of claim 11, wherein the 279Arg MMP-9 enzyme is purified enzyme.

16. The method of claim 14, wherein the 279Arg MMP-9 enzyme and the 279Gln MMP-9 enzyme are each purified enzyme.

17. The method of claim 14, wherein the gene expressing the 279Gln MMP-9 enzyme is SEQ ID NO:11 where 841 n is adenine (A).

20 18. A method of determining the efficacy of a substance to inhibit a 279Arg MMP-9 enzyme without substantially inhibiting a 279Gln MMP-9 enzyme for use as a therapeutic or preventive agent for COPD, the method comprising the steps of:

providing the 279Arg MMP-9 enzyme;  
testing the substance for inhibition of the 279Arg MMP-9 enzyme;  
providing the 279Gln MMP-9 enzyme;

25 testing the substance for inhibition of the 279Gln MMP-9 enzyme;  
comparing the results obtained for inhibition of the 279Arg MMP-9 enzyme with results obtained for inhibition of the 279Gln MMP-9 enzyme; and  
selecting the substance which inhibits the 279Arg MMP-9 enzyme without substantially inhibiting the 279Gln MMP-9 enzyme.

19. The method of claim 18, wherein providing the 279Arg MMP-9 enzyme and the 279Gln MMP-9 enzyme comprises inserting a gene expressing the 279Arg MMP-9 enzyme into a first cell line and inserting a gene expressing the 279Gln MMP-9 enzyme into a second cell line.

20. The method of claim 19, wherein the gene expressing the 279Arg MMP-9 enzyme is  
5 SEQ ID NO:11 where 841 n is G and the gene expressing the 279Gln MMP-9 enzyme is SEQ ID  
NO:11 where 841 n is A.

21. The method of claim 18, wherein the 279Arg MMP-9 enzyme and the 279Gln MMP-9 enzyme are each purified enzyme.

22. A method of treating a patient with COPD or at risk for developing COPD, comprising  
10 the steps of:

determining the presence of an exon 6 codon 279 Gln/Arg single nucleotide polymorphism within the MMP-9 locus in a biological sample obtained from the patient;

administering an MMP-9 inhibitor to the patient with a 279 arginine polymorphism.

23. The method of claim 22, wherein the MMP-9 inhibitor is a selective 279Arg MMP-9  
15 enzyme inhibitor.